DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

Government-Owned Inventions; Availability for Licensing

AGENCY: National Institutes of Health, Public Health Service, DHHS.

ACTION: Notice.

SUMMARY: The invention listed below is owned by an agency of the U.S. Government and is available for licensing in the U.S. in accordance with 35 U.S.C. 207 to achieve expeditious commercialization of results of federally-funded research and development. Foreign patent applications are filed on selected inventions to extend market coverage for companies and may also be available for licensing.

ADDRESSES: Licensing information and copies of any U.S. patent applications listed below may be obtained by writing to the indicated licensing contact at the Office of Technology Transfer, National Institutes of Health, 6011 Executive Boulevard, Suite 325, Rockville, Maryland 20852–3804; telephone: (301) 496–7057; fax: (301) 402–0220. A signed Confidential Disclosure Agreement will be required to receive copies of the patent applications.

Human UGRP1 (Uteroglobin-Related Protein 1) Promoter and Its Use

Shioko Kimura and Tomoaki Nimi (NCI). PCT Application No. PCT/US02/19456 filed 18 Jun 2002 (with priority to 20 Jun 2001), which published as W0 03/000111 on 03 Jan 2003 (DHHS Reference No. E–058–2001/0–PCT–02). Licensing Contact: Susan Carson; (301) 435–5020; carsonsu@mail.nih.gov.

Asthma is a genetically complex, multi-factorial disease affecting more than 17 million people in the United States alone and costing approximately US$6 billion to treat annually. Identification, mapping and linkage analyses of Single Nucleotide Polymorphisms (SNPs) have been increasingly used both to study the genetic etiology of asthma and to detect genetic loci contributing to asthma susceptibility. Researchers from the National Cancer Institute have described a novel gene, located in an asthma-susceptibility gene loci 5q31–34, named UGRP1 (uteroglobin-related protein 1) and an associated polymorphism that is significantly associated with asthma (Nimi *et al.* (2002) Am. J. Hum. Genet 70: 718–725).

UGRP1 is a homodimeric secretory protein of ~10 kDA and is expressed only in lung and trachea. The –112G/A polymorphism was identified in the human UGRP1 gene promoter and is responsible for a 24% reduction in the promoter activity in relation to the –112G allele, as examined by transfection analysis. In a case-control study using 169 Japanese individuals (84 with asthma and 85 unrelated healthy controls) those with a –112A allele (G/A or A/A) were 4.1 times more likely to have asthma than were those with the wild-type allele(G/G).

The invention describes the –112G/A polymorphism and the UGRP1 promoter region as well as methods for detecting polymorphisms present in the UGRP1 promoter which can be used as indicators for diagnosing or for predicting a predisposition to develop a respiratory disorder. The complex and polygenic nature of asthma suggests that this potential asthma susceptibility allele can be of great value not only to companies targeting respiratory diseases such as asthma but also to those more broadly involved in gene discovery, gene mapping, association-based candidate polymorphism testing, pharmacogenetics, diagnostics and risk profiling.

Dated: December 1, 2003.

Steven M. Ferguson,

Director, Division of Technology Development and Transfer, Office of Technology Transfer, National Institutes of Health.

[FR Doc. 03–30497 Filed 12–8–03; 8:45 am]

BILLING CODE 4140–01–P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

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Construction of Replication-Competent Chimeric Simian Immunodeficiency Virus (SIV) Human Immunodeficiency Virus Type 1 (HIV–1) Viruses that Replicate Using HIV–1 Reverse Transcriptase and Integrase (IN): A Model System for Development and Testing of Antiviral Agents for the Treatment of HIV–1 Infection

Vijay K. Pathak and Yijun Zhang (NCI). DHHS Reference No. E–019–2004/0—Research Tool. Licensing Contact: Michael Ambrose; (301) 594–6565; *ambrosea@mail.nih.gov.*

Currently antiviral therapy is based on a cocktail that inhibits viral replication. These drugs are targeted toward the Reverse Transcriptase (RT) enzyme to inhibit such replication. However, development of HIV drug resistance to these current therapies is the leading blockage to successful treatment of such patients, and as such, leads to the progression of AIDS and eventual death. The goal of developing successful next generation drugs for HIV must contend with (1) the alarming rate of mutation of HIV and (2) an animal model that represents the natural disease in humans. This latter point must also have as one of its properties; the natural occurring mutation and resistance to the therapy in develop.

To address these questions, a chimeric virus was developed between SIV and HIV. The SIV backbone is altered such that the HIV RT and Integrase (IN) enzymes are expressed in infected cells. This allows the use of the macaque as the animal model and having the RT and IN of HIV as the potential drug targets. In this system, novel therapies can be developed and studied in vivo, in single or in combination form, in a manner more similar to the human HIV infection then is currently available. Further, toxicity studies can be designed and results obtained that are more relevant to the human disease condition.

One other advantage is the ability to use the macaque model to discover additional generations of HIV therapies and tested in the same system. This provides identical biological backgrounds to address toxicity concerns of changing medications as one becomes resistant and newer therapies are administered.

HIV–1/SIV Chimeras Promoting Trimerization of Soluble HIV–1 ENV

Bernard Moss (NIAID). U.S. Provisional Application filed 10 Oct 2003 (DHHS Reference No. E–356–2003/0–US–01). *Licensing Contact:* Susan Ano; (301) 435–5515; *anos@mail.nih.gov.*

The technology describes the replacement of the gp41 segment of HIV–1 gp140 or just the N-terminal portion (85 amino acids) with the corresponding region of SIV to promote efficient trimerization. Functional, virion associated HIV–1 and SIV env have been shown to have an almost exclusively trimeric structure. The chimera that contains only the N-terminal portion of SIV in an HIV–1 background is particularly interesting, since several broadly neutralizing HIV–1 epitopes are present in the C-terminal segment of gp41. Thus, the current technology could be useful as an immunogen to elicit antibodies that recognize a mimic of the native trimeric structure. The region of HIV–1 replaced by SIV sequence contains no known targets of neutralizing antibodies.

Use of a Statin To Kill EBV-Transformed B Cells

Jeffrey Cohen *et al.* (NIAID). U.S. Provisional Application filed 28 Oct 2003 (DHHS Reference No. E–312–2003/0-US–01).

Licensing Contact: Susan Ano; (301) 435–5515; *anos@mail.nih.gov.*

This technology describes the use of certain natural and synthetic statins, including simvastatin, other leukocyte function antigen–1 (LFA–1) inhibiting statins, and compounds derived from LFA–1 inhibiting statins and statin-like compounds, for treatment or prevention of Epstein-Barr Virus (EBV) associated tumors, including lymphomas that express LFA–1 and transforming proteins. Such compounds could also be used to treat tumors associated with other viruses that express LFA–1. Cancers associated with EBV that could be treated with the statins by methods described herein include naspharyngeal carcinoma, Hodgkin's disease, lymphoproliferative disease, T-cell lymphoma, and non-Hodgkin's lymphoma.

HIV-Dependent Expression Vector

Drs. Jon Marsh and Yuntao Wu (NIMH). U.S. Provisional Application No. 60/507,034 filed 28 Sep 2003 (DHHS Reference No. E–276–2003/0-US–01).

Licensing Contact: Sally Hu; (301) 435–5606; *hus@mail.nih.gov.*

This invention provides a DNA construct that can be useful for both diagnostics and AIDS therapeutics. The construct can be incorporated into a retrovirus or into a cell line. This construct mediates the expression of a selected gene in the presence of HIV replication, but is silent in the absence of HIV. The cell line with the incorporated construct can be used as an indicator line for the presence of replication-competent HIV. The virus containing the construct can be used to co-infect a population of HIV-infected cells. If the construct-encoded gene is a reporter, it would specifically identify cells that are infected with HIV. If the construct-encoded gene is a cytotoxin, it would specifically kill cells that are HIV-infected. This invention may offer a novel approach to HIV elimination, as well as detection of HIV infected cells or the presence of cell-free infectious HIV.

Polypeptide Multimers Having Antiviral Activity

Carol Weiss *et al.* (FDA). PCT Application filed 14 Aug 2003 (DHHS Reference No. E–155–2003/0-PCT–01); U.S. Patent Application No. 09/480,336 filed 07 Jan 2000 (DHHS Reference No. E–212–2001/0-US–02).

Licensing Contact: Susan Ano; (301) 435–5515; *anos@mail.nih.gov.*

The technology describes polypeptide multimers that have antiviral and immunogenic activity against HIV. These multimers consist of at least one monomer of the highly conserved N and C heptad regions of gp41 in a ratio of at least 2:1 N to C heptad, with the N and C heptads being connected by linkers. The monomer forms homodimers and homotrimers in solution and mimic fusion intermediate structure. Further, the technology also describes a method of raising a broadly neutralizing antibody response to HIV by administering the polypeptide multimers mentioned above. Thus, these polypeptide multimers may be used as antiviral (anti-HIV) agents. Because the structure of these polypeptide multimers mimics the gp41 fusion intermediate, they can also be used to identify compounds that may inhibit the fusion process.

Discovery of Novel Inhibitors of HIV–1 Integrase and/or RNase H That Can Be Used for the Treatment of Retroviral Infection Including AIDS

Stuart F. J. Le Grice (NCI) *et al.* U.S. Provisional Application filed 31 Oct 2003 (DHHS Reference No. E–022–2003/0-US–01).

Licensing Contact: Sally Hu; (301) 435–5606; e-mail: *hus@mail.nih.gov.*

This invention provides compounds and methods of treating retroviral infection such as AIDS by administration of a dioxtetrahydrobenzo[a]naphthacene compound, particularly a 8,13-dioxo-5,6,8,13-tetrahydro-benzo[a]naphthacene compound, *i.e.* a madurahydroxylactone compound. Retroviruses, such as HIV, need three viral enzymes for replication: reverse transcriptase, protease, and integrase. The prognosis of AIDS patients has recently been improved by the discovery and associated therapeutic administration of reverse transcriptase and/or protease inhibitors. However, a significant portion of AIDS patients fail to respond to such treatments and viral resistance remains a major problem.

It is known that HIV–1 integrase is a rational target for AIDS therapy because genetic studies have demonstrated that the enzyme is essential for viral replication, and because there is no cellular equivalent. On the other hand, the reverse transcriptase RNase H active site is another good target for antiviral therapeutic development because elimination of the RNase H activity of reverse transcriptase arrests virus replication. The compounds reported in this invention may be capable of inhibiting both enzymes since the catalytic centers of integrase and RNase H are structurally similar. As a consequence, this invention can potentially avoid viral resistance, which limits the efficacy of presently administered reverse transcriptase and/or protease inhibitor therapeutic agents. Thus, the invention may be a group of new small molecule agents for treating patients suffering from retroviral infections, particularly patients suffering from Human Immunodeficiency Virus (HIV).

Particles for Imaging Cells

Kathleen Hinds, Cynthia Dunbar (NHLBI). U.S. Patent Application No. 10/313,304 filed 06 Dec 2002 (DHHS Reference No. E–185–2002/0–US–01).

Licensing Contact: Michael Shmilovich; (301) 435–5019; shmilovm@mail.nih.gov.

Available for licensing are NIH patent pending contrast particles for use in MRI and flow cytometry to track cells migration in real time. Present cell-tracking studies rely on labeling cells with ultra-small dextran-coated iron particles that are endocytosed. The contrast agent of the present invention uses larger iron oxide particles, approximately 1 μm, situated in a tri-layer structure. The inner structure is a magnetic molecular complex of FITC (a fluorescent marker) encased in a layer of superparamagnetic microparticles, which is then covered with a shell of

inert polystyrene and di-vinyl benzene coated with soluble -COOH groups. Accordingly, the particle is labeled with both a magnetic and fluorescent marker. This dual labeling permits monitoring of the molecule on multiple spatial scales, from intracellular distribution to distribution throughout the animal.

Methods for Detecting Cancer Cells

Thomas Ried, Evelin Schrock, Bijan M. Ghadimi (NHGRI). U.S. Provisional Application No. 60/127,637 filed 01 Apr 1999 (DHHS Reference No. E–211–1998/0–US–01); PCT Application No. PCT/US00/08588 filed 31 Mar 2000 (DHHS Reference No. E–211–1998/0–PCT–02); U.S. Patent Application No. 09/937,864 filed 31 Dec 2000 (DHHS Reference No. E–211–1998/0–US–03). *Licensing Contact:* Michael Ambrose; (301) 594–6565; *ambrosem@mail.nih.gov.*

The present application describes a highly sensitive assay for distinguishing between cancer and non-cancer epithelial cells in the blood. It provides an improved diagnostic technique for detecting cancer and determining the organ-origin of the cancer. This assay can be used to prove the neoplastic nature of cells and predict when shed tumor cells have or will become metastatic. A major advantage of the present invention is that tumor cells can also be recovered as viable cells. Thus, the tumor cells can be kept alive in vitro for a sufficient period of time to determine the effect of particular anti-tumor pharmaceuticals on the cells. Furthermore, the assay provides an early detector of treatment success or failure and thereby allows a treatment regimen to be customized for an individual patient with advanced primary cancer.

Method for Detecting Transmissible Spongiform Encephalopathies

Gary E. Hsich, Kimbra Kenney, Clarence J. Gibbs, Michael G. Harrington (NINDS). U.S. Patent 5,998,149 issued on 07 Dec 1999 (DHHS Reference No. E–055–1996/0–US–01); U.S. Patent 6,406,860 issued on 18 Jul 2002 (DHHS Reference No. E–055–1996/0–US–02). *Licensing Contact:* Michael Ambrose; (301) 594–6565; *ambrosem@mail.nih.gov.*

Improved assays for the detection of transmissible spongiform encephalopathies (TSEs) in humans and non-human mammals have been developed. The assays involve detecting the presence or absence of 14–3–3 proteins in cerebrospinal fluid. Elevated levels of these proteins are indicative of TSEs, in particular Creutzfeldt-Jacob disease in humans and animals with these diseases. This invention is available for licensing on a non-exclusive basis.

Dated: December 1, 2003.

Steven M. Ferguson,

Director, Division of Technology Development and Transfer, Office of Technology Transfer, National Institutes of Health.

[FR Doc. 03–30498 Filed 12–8–03; 8:45 am]

BILLING CODE 4140–01–P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

National Institute of Neurological Disorders and Stroke; Notice of Closed Meetings

Pursuant to section 10(d) of the Federal Advisory Committee Act, as amended (5 U.S.C. Appendix 2), notice is hereby given of the following meetings.

The meetings will be closed to the public in accordance with the provisions set forth in sections 552b(c)(4) and 552b(c)(6), Title 5 U.S.C., as amended. The grant applications and the discussions could disclose confidential trade secrets or commercial property such as patentable material, and personal information concerning individuals associated with the grant applications, the disclosure of which would constitute a clearly unwarranted invasion of personal privacy.

Name of Committee: National Institute of Neurological Disorders and Stroke Special Emphasis Panel, Steroid Receptor Chaperones in Axonal Elongation.

Date: December 11, 2003.

Time: 8:30 am to 9:30 am.

Agenda: To review and evaluate grant applications.

Place: Ritz-Carlton Hotel at Pentagon City, 1250 South Hayes Street, Arlington, VA 22202, (Telephone Conference Call).

Contact Person: W. Ernest Lyons, PhD, Scientific Review Administrator, Scientific Review Branch, NINDS/NIH/DHHS, Neuroscience Center, 6001 Executive Blvd., Suite 3208, MSC 9529, Bethesda, MD 20892–9529, (301) 496–4056.

This notice is being published less than 15 days prior to the meeting due to the timing limitations imposed by the review and funding cycle.

Name of Committee: National Institute of Neurological Disorders and Stroke Special Emphasis Panel, Molecular Regulation of Neural Migration.

Date: December 11, 2003.

Time: 10 am to 3:30 pm.

Agenda: To review and evaluate grant applications.

Place: Ritz-Carlton Hotel at Pentagon City, 1250 South Hayes Street, Arlington, VA 22202.

Contact Person: W. Ernest Lyons, PhD, Scientific Review Administrator, Scientific Review Branch, NINDS/NIH/DHHS, Neuroscience Center, 6001 Executive Blvd., Suite 3208, MSC 9529, Bethesda, MD 20892–9529, (301) 496–4056.

This notice is being published less than 15 days prior to the meeting due to the timing limitations imposed by the review and funding cycle.

Name of Committee: National Institute of Neurological Disorders and Stroke Special Emphasis Panel, Program in Cognitive Neuroscience.

Date: December 18, 2003.

Time: 1 pm to 2:30 pm.

Agenda: To review and evaluate grant applications.

Place: National Institutes of Health, Neuroscience Center, 6001 Executive Boulevard, Rockville, MD 20852, (Telephone Conference Call).

Contact Person: Richard D. Crosland, PhD, Scientific Review Administrator, Scientific Review Branch, Division of Extramural Research, NINDS/NIH/DHHS, Neuroscience Center, 6001 Executive Blvd., Suite 3208, MSC 9529, Bethesda, MD 20892–9529, 301–594–0635.

This notice is being published less than 15 days prior to the meeting due to the timing limitations imposed by the review and funding cycle.

Name of Committee: National Institute of Neurological Disorders and Stroke Special Emphasis Panel, NeuroAIDS Imaging Studies.

Date: January 8, 2004.

Time: 8 am to 5 pm.

Agenda: To review and evaluate grant applications.

Place: The Fairmont Washington, DC, 2401 M Street, NW, Washington, DC 20037.

Contact Person: Andrea Sawczuk, DDS, PhD, Scientific Review Administrator, Scientific Review Branch, Division of Extamural Research, NINDS/NIH/DHHS, 6001 Executive Boulevard, Room #3208, Bethesda, MD 20892, (301) 496–0660, *sawczuka@ninds.nih.gov.*

(Catalogue of Federal Domestic Assistance Program Nos. 93.853, Clinical Research Related to Neurological Disorders; 93.854, Biological Basis Research in the Neurosciences, National Institutes of Health, HHS)

Dated: December 4, 2003.

Anna Snouffer,

Acting Director, Office of Federal Advisory Committee Policy.

[FR Doc. 03–30494 Filed 12–8–03; 8:45 am]

BILLING CODE 4140–01–M

DEPARTMENT OF HOUSING AND URBAN DEVELOPMENT

[Docket No. FR–4630–FA–11B]

Announcement of Funding Award—FY 2001 Healthy Homes Grant Program

AGENCY: Office of the Secretary—Office of Healthy Homes Research Grant Program.